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AUTHOR Jaranson, James M.
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ABSTRACT

This paper is an overview of issues and findings in the use of medication to treat mentally ill refugees. The introductory background section briefly discusses the development of interest in ethnic differences in response to psychotropic drugs. The second section highlights the results of research literature on the use of the following kinds of drugs with Asian refugees: antidepressant medication, antipsychotic medication, anti-anxiety medication, and lithium. The paper goes on to assess some of the methodological difficulties in conducting sound research and to review possible explanations for ethnic differences in response to psychotropic drugs, including genetic and environmental considerations along with biological, psychological, and socio-cultural considerations. The issue of noncompliance with prescribed medications is also addressed, general principles of clinical treatment are outlined, and recommendations for research are offered. References are included. (TE)

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PSYCHOTHERAPEUTIC MEDICATION IN THE TREATMENT OF REFUGEES

James M. Jaranson, M.D., M.A., M.P.H.
Assistant Professor
Department of Psychiatry
University of Minnesota
at St. Paul-Ramsey Medical Center

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PSYCHOTHERAPEUTIC MEDICATION IN THE

TREATMENT OF REFUGEES

Discussion of the use of medication to treat mentally ill refugees is often neglected in the refugee literature. Instead, much of the literature about differences in response to psychotropic drugs among ethnic or cultural groups is found in publications from the fields of transcultural psychiatry or pharmacology. To synthesize the findings is difficult not only because they are reported in a wide variety of journals reflecting differing perspectives, but also because refugee status and ethnicity are often intertwined. In part, this is explained by the overlap of ethnicity with refugee status since so many of the refugees today come from "third world" or more traditional societies and are often non-Caucasian. Responses to medication differ depending upon those factors and upon many biodemographic variables such as age, sex, or length of time in the country of resettlement. Studies do not include all refugees from all ethnic groups stratified by age or sex. The literature in the United States, for example, primarily discusses Asian adults, most of whom are not even refugees.

In this context, making recommendations for treatment or research is risky and suggestions are subject to limitations of generalizability. Guidelines are needed, especially for treatment, but the most useful information comes from collective experience rather than from carefully designed clinical research studies. Treatment guidelines need to be specific but then risk a "cookbook" approach or contradict the wisdom of some expert clinicians.

This paper will briefly discuss the development of interest in ethnic differences to psychotropic drugs, highlight results from the research literature, comment on methodological difficulties in conducting sound research, review possible explanations for ethnic differences, suggest general principles to follow when treating refugees and those from other ethnic or cultural groups, and identify research needs and strategies. The intended audience includes clinicians and others providing care for refugees with mental illness in the United States.

BACKGROUND OF THE FIELD

Knowledge about the pharmacologic treatment of mental illness in refugees comes from two very different fields: psychiatry and pharmacology, each with a different origin, history, and philosophical orientation.

The possibility of ethnic differences in response to psychotherapeutic medications originally came from observations that American psychiatrists used higher doses of neuroleptics to treat schizophrenics than did Europeans who, in turn, used more than clinicians in developing countries (Lewis, 1980). These same patterns held for antidepressants and anti-anxiety agents, but the evidence was often antedoctal and did not control for diagnostic variables or other factors such as availability of medications.

In pharmacology, following the availability of many effective medications in the middle of the twentieth century, awareness of individual differences in drug response led to the development of the field of pharmacogenetics more than thirty years ago (Kalow, 1986a). Subsequently, variation among individuals in response to environmental contaminants led to an interest in ecogenetics. Concurrently, enzyme induction and adaptation were becoming linked to environmental factors.

Most recently, the preoccupation with inter-individual differences has been followed by an interest in inter-ethnic differences, or differences between defined populations. Kalow (1984) prefers to call this study "pharmacoanthropology," requiring knowledge of drugs or medications (as well as environmental poisons) and analysis of the physical and cultural characteristics of humans in or from geographical areas (Kalow, 1986b).

The basic research question for pharmacoanthropology is well-formulated by Chrusciel (1978): "To what extent and how frequently are there changes in response to psychotropic drugs by sick people of different genetic backgrounds living in different environmental conditions?" Chrusciel couches this basic question in his article aptly entitled "Questions We Recognize But Cannot Formulate." In actuality, this question is a series of closely related questions which are difficult to operationalize for research purposes.

Research in this subject area has been reviewed in the 1980's by both British (Lewis, 1980) and American (Lin, 1986a) authors. While the earlier research focused on comparative doses and side effects of various categories of psychotropic medication, only more recently have

biological correlates such as tricyclic antidepressant blood levels or EEG responses been used to support the data. The most impressive body of literature is found comparing Asian patients to other groups, usually Caucasian (Lin, 1984, 1986b; Acosta, 1982). Although only a few of these studies directly involve Southeast Asian refugees, the largest refugee groups in America today, comparison of differences between Asian and Caucasian groups should have some relevance in the treatment of refugees.

RESULTS OF RESEARCH LITERATURE

Although most of the research has studied differenes in response on a pharmacologic or clinical level, it should be emphasized that the similarities between individuals and between population groups are perhaps greater than the differences. When differences in treatment response or emergence of side effects are documented, the variation from one individual to the next within a given population is usually greater than between the ethnic populations studied. Not only are there many drugs which could be studied, but multiple factors affect the metabolism of each one of these drugs. When differences are found, they appear to be primarily quantitative rather than qualitative and the reasons for such differences are not clearly understood. Nonetheless, evidence continues to indicate that selected ethnic groups, including those to which many refugees belong, either respond therapeutically to or can only tolerate lower doses of psychotropic medication. The following sections will discuss relevant research results in each of these psychotropic drug categories.

Antidepressant Medication

By far the largest number of articles in the pharmacoanthropology literature studies involve antidepressant medication. In a multi-national survey, Yamashita (1979) discovered that amitriptyline and imipramine were used in much lower doses in Asian countries than in the United States. Yamamoto (1979) noted similar findings comparing both Asians and Caucasians in the United States. Pi (1986) and Rudorfer (1984) found that Asians reached peak plasma levels of antidepressants earlier than Caucasians. Rudorfer found that the plasma clearance of desipramine was lower in Asians and consequently the blood level of the antidepressant remained higher in Asians even though they were given the same dose as Caucasians. Pi (1986) failed to find such a difference and this was corroborated in Southeast Asians by Kinzie (1987). In another study using clomipramine in fixed single oral doses, blood levels of Asian groups several hours later were much higher than for an English comparison group.

Other studies have indicated that therapeutic dosage requirements for Hispanics and Blacks are lower than for Caucasians. Marcos (1982) found that Puerto Ricans required about one half of the dosage of Caucasian patients but reported twice as many side effects. However, Gaviria (1986) found that Mexican-American and Caucasian volunteers showed no difference in the pharmacokinetic parameters, maintaining similar blood levels with similar doses of nortriptyline. Ziegler (1978) reported that amitriptyline (Elavil) reached higher blood levels

and that clinical improvement was faster in Black patients compared with Caucasian patients given comparable doses. Consequently, clinically-based reports show differences between various ethnic groups more frequently than do the studies involving blood levels for antidepressants.

Antipsychotic Medications

International comparison studies have shown that the average prescribed dosage of neuroleptics varies greatly from one country to the next. For example, Potkin (1984) noted that in receiving the same fixed dose of haloperidol (Haldol) for six weeks, plasma levels of Chinese schizophrenic patients in Peking were more than 50% higher than levels of schizophrenics in the United States. Lin (1984) found similar results after administering a test dose to volunteer subjects. In the United States, Yamamoto (1979) found that American Asians in Los Angeles responded to very low doses of neuroleptics, replicating many findings in the international literature. Lin's data (1983) found that hospitalized patients also responded differentially, with Asian patients requiring far lower doses of neuroleptics than Caucasians for clinical improvement. Sramek (1986), however, failed to replicate Lin's 1983 study, stating that no significant difference in the neuroleptic dose requirements of Asian and Caucasian psychiatric patients was found. The latter author believes that doses were prescribed to various ethnic groups based upon preconceived ideas of the requirements instead of the actual clinical need. Binder (1981) studied the side effects of the antipsychotic medication for a comparison group of Black and Caucasian patients with Asians and discovered that extrapyramidal reactions were far more frequent in Asian patients.

Antianxiety Medications

Ghoneim (1981) compared sedative effects of diazepam (Valium) in Caucasians and Asians and found no difference. However, the clearance of Valium was higher in Caucasians, resulting in higher blood levels for the Asians. Their conclusion was that Valium was metabolized at a much lower rate in Asians. Lin has studied alprazolam (Xanax) in a similar fashion.

Lithium

In Japan, Takahashi (1979) reported that many manic depressive patients responded to low doses of Lithium and this was corroborated by Yang (1985) in Taiwanese manic depressive patients. Other notable effects were that similar blood levels were achieved with similar doses and that the medication was apparently metabolized at the same rate in these Asian groups compared with Caucasians. However, the studies consistently indicate that Asian manic depressive patients respond to lower blood levels of lithium, indicating that the brain receptors may respond differently in these ethnic groups.

Assessment of the Research Literature

Although there is considerable published literature discussing differences in dosage requirements and in side effects for various ethnic groups, many methodologic problems are present. First of all, seldom are either the comparison groups or the study groups homogeneous culturally or ethnically. When the studies are cross-national, diagnostic criteria often vary. Factors such as chronicity, severity of

illness, and prior treatment history are problematic. Many of the studies are retrospective rather than prospective and poorly controlled. Only recently have blood levels of the antipsychotics or antidepressants been used to determine whether differences were based on the metabolism of the medication or on other factors. Despite these methodologic inconsistencies, it does appear that many Asians respond psychotherapeutically to lower doses of antipsychotic and antidepressant medication, at least for the older and more frequently studied medications. Hispanics and Blacks may respond to lower doses of antidepressant medication but antipsychotic medications have not been carefully studied in these groups.

Explanations for the Ethnic Differences

1. Genetic and Environmental Considerations

Many genetic and environmental factors are likely responsible for differences among ethnic groups. Considerable work has been completed in pharmacogenetics, and carefully designed studies using twins have shown bio- chemical differences. Relatively more recently environmental factors have been considered to be of importance.

It has always been difficult to separate nature (or genetic factors) from nurture (or environmental factors) and this remains true in pharmaco anthropology. For population research to determine differences between ethnic groups, it would make sense to compare a carefully defined ethnic group in one geographic location with a similar group in another geographic location. This was done in several cross-national studies,

for example, comparing the incidence of heart disease in Japanese and in Japanese-Americans. These results showed that the rate of heart disease of Japanese-Americans was more similar to Caucasian-Americans than to those Japanese who had remained in Japan. Similar findings studied the drug Antipyrine in Sudanese and in those Sudanese who had immigrated to England (Brauch 1978). The immigrants had metabolic parameters of the medication which were much more similar to the English than to the Sudanese who had remained in Sudan.

Most of the contributions of pharmacogenetics to drug differences are on an individual rather than a population basis, and many results come from carefully controlled assessments of differences in the rate of metabolism of various substances. For example, it has long been noted that acetylation varies considerably. In one case, this is due to a deficiency in aldehyde dehydrogenase, causing alcohol intolerance, facial flushing and cardiovascular symptoms. This has an incidence of 30-50% in various Oriental groups and is is inherited in an autosomal dominant fashion. For antidepressants, such as phenelzine (Nardil), slow acetylation is due to defective determinant in acetyltransferase. The incidence in Caucasians and Blacks is nearly 60% while only 10-20% in Orientals. The mode of inheritance is autosomal recessive. For nortriptyline, hydroxylation deficiency has been discovered. Orientals metabolize the antidepressant poorly in 30% of the cases compared with 6-9% of Caucasians. This is inherited in an autosomal recessive manner (Goedde, 1986).

Environmental factors are clearly important and recognized as increasingly important in pharmacoanthropology. Such factors include diet and nutrition, perhaps the most important environmental influences (Anderson, 1986). Besides diet, factors such as climate, atmospheric pollution, cigarette smoking, previous exposure to other drugs or food additives, the economic state of the individual, the level of sanitation, the educational level, and so forth are important considerations in the assessment of responses by various ethnic groups to medications. The following section will discuss biopsychosocial factors which can explain differences in responses to medication and are also influenced by both genetic and environmental factors.

2. Biopsychosocial Considerations

Biological Parameters

Advances within pharmacology enable categorization of the mechanisms of action of the medications as either pharmacodynamic or pharmacokinetic. Ethnic variability in dosage requirements can be based upon differences in brain receptors (dynamics) or body metabolism (kinetics). Even if the same dose of medication results in the same blood levels in different ethnic groups (kinetics), the dose requirements for therapeutic response may vary depending upon differing responses in the brain (dynamics). The research evidence is conflicting as to which mechanism determines the ethnic variation. For example, desipramine and diazepam have shown higher peak blood levels in Asians than in Caucasians (Rudorfer 1984, Ghoneim 1981). However, Gaviria (1986), Kinzie (1987), and Pi (1986) found that blood levels of

nortriptyline, imipramine, and desipramine are comparable at identical doses in both Asian and Caucasian groups. The latter findings would indicate that the pharmacodynamic (or brain receptor) considerations are more important. It has also been noted that levels of Lithium for Japanese patients are much lower to achieve a therapeutic result than in Caucasians and this would also suggest a pharmacodynamic explanation for ethnic differences (Takahashi, 1979).

Both genetic and environmental control of these biological mechanisms is possible. For example, enzyme systems are genetically controlled but prior experience with substances such as smoking (Linnoila, 1981)or barbiturates, which increase the activity of these enzymes, are environmental factors of consequence. Finally, the biological consideration of the disease itself is important. Some of the research studies have been completed on volunteers rather than psychiatrically ill patients. There is, considerable evidence that psychiatrically ill patients differ biochemically from those who are normal and this calls in the question of validity of those studies which use only volunteers.

Research studying ethnic variation in response to psychotropic medications has often neglected biological parameters such as body weight and fat distribution, failing to control these in different ethnic populations. Since many of the medications are stored in the fat tissue, this is an extremely important consideration.

Psychological Parameters

Considerable research has been completed on the response of personality types to various medications. Heninger (1965) noted that Type A subjects react very negatively to chlorpromazine (Thorazine), demonstrating more sleepiness, impairment and confusion compared with Type B subjects. Slater (1966) noted that patients responding to either stimulants (amphetamines) or tranquilizers (Mellaril) had paradoxical reactions if they were more trusting and compliant rather than dominant or energetic. In a study by McDonald (1967) Valium had a paradoxical reaction in volunteer females who were hostile, anxious, and depressed. Frostad (1966) found similar results. It should be noted that most of this research was done in the 1960s and the interest in this area seems to have waned, but it is likely that certain personality types are more frequent within different ethnic cultures. This may have a significant influence on the response to medication.

Socio-Cultural Parameters

Social and cultural expectations for both the provider and the patient, and the communication between physician and patient, may significantly influence factors such as medication compliance. Kinzie (1985) states that the expectations of Western providers and Asian patients are often very similar, and, consequently, a medical model for treatment seems to work well (Table 1). However, in many Southeast Asian groups it is clear that both the understanding of the concept of illness causation and the expectations for medication response differ considerably. For example, the concept of chronic disease and the need

to take maintenance medication over a long period of time is not well accepted in Southeast Asian groups. In addition, medication is often shared with family members who may have similar problems, there is seldom rigid adherence either to dosage or to time intervals, and patients frequently expect that the length of treatment will be short. Patients may feel that the more often that they take medication the faster their symptoms will improve. On the other hand, they may forget medications which are regularly scheduled on a regular basis because they are not informed of the importance of taking them regularly.

There are also many differences between characteristics of traditional and modern medical systems (Table 2). Depending upon the level of industrial development, the relative dependence upon traditional healing approaches and concepts will vary. It may be expected, for example, that the Hmong and Mien would have a much more traditional view of the world and medicine than most Vietnamese, who have had more contact with the West.

These sorts of expectations may have significant influence on the tolerance of the individual patient to symptoms. For example, as noted by Acosta (1982), some of the side effects of psychotropic drugs include akinesia, characterized by weakness of the muscles and limbs. This side effect can easily be misinterpreted by Asian patients as a deficiency in vital strength or energy and may cause some to seek help through herbal remedies. Consequent interactions between herbal medicines and psychotropic medication sometimes can be dangerous or at least confound treatment.

Medication Compliance Issues

High rates of non-compliance with prescribed medications have been reported in the literature. Among mainstream populations, non-compliance rates have ranged from 15-94% (Masur, 1981). One might expect even higher rates of non-compliance among refugee groups, for whom cultural and communication barriers are especially great. Kinzie (1987) has recently affirmed this expectation in a study of Cambodian, Vietnamese, and Mien patients at the Oregon Health Sciences University. He monitored tricyclic antidepressant blood levels for 41 patients, finding that only 39% had detectable levels of medication. The Cambodians had detectable levels much more frequently than the other two groups, indicating greater compliance. The findings were notably contrasted with 80% compliance for keeping appointments. After education of patients and Indochinese mental health counselors was provided, non-compliance fell from 61% to 37%, most significantly in the Vietnamese group. The Mien compliance rate of 67% remained virtually unchanged. Kinzie notes that the Mien have had the greatest cultural gap to bridge by coming to the United States and often believe more in the supernatural. For the Cambodians, Kinzie notes that the greater compliance may have been due to more rapid acceptance of Western illness concepts or to greater impairment by chronic post-traumatic stress disorder, with consequent relief of insomnia and nightmares from the medication.

Socio-cultural issues related to medication compliance have been mentioned previously in this paper. Side effects of the medications, such as akinesia, but also excessive sedation, dizziness, dry mouth, or

constipation, affect compliance rates. Other factors contributing to poor medication compliance include communication barriers such as language and lack of clear instruction. For many, if not for most, of the Southeast Asian groups, the language barrier is one of the most difficult to overcome and, consequently, well informed interpreters or bilingual counselors are of critical importance.

Instruction is needed, not only the details of taking the medication, such as how much, at which times of the day, and for how long, but also the reasons for taking the medication as prescribed. Finally, economic considerations are prohibitive for many refugees. Some prescriptions are not reimbursed by public or private payors and the ability to pay out of pocket is frequently limited.

General Principles of Clinical Treatment

Although there is not universal agreement regarding treatment approaches, certain principles can be proposed based upon review of the literature and upon the clinical experience of those who are in the field of refugee mental health. Some of the principles, of course, overlap with and reiterate basic tenets of good clinical psychiatry.

The following principles present the consensus of the literature and formal discussions with psychiatrists who have committed a significant portion of their careers over many years to treat mentally ill refugees.

1. Diagnostic assessment and evaluation should ideally be completed prior to starting treatment with psychotherapeutic medication. However, it is often necessary to treat target symptoms rather than DSM-III-R syndromes in order to provide distressed patients some relief, develop a trust level, and enable greater participation in other forms of therapy. Sometimes it takes much longer to complete a diagnostic assessment in refugees due to language barriers, differing conceptions of the illness, and unusual presentations of symptom complexes. For example, depression will often be presented by the patient as somatic complaints (Lin, 1984). In addition, post-traumatic stress disorder is a frequent diagnosis but rarely seen without co-existence of another Axis I diagnosis such as depression or anxiety. Organic brain syndrome often may be diagnosed only much later in treatment, frequently after a complete neurologic evaluation.

2. Maximizing compliance is critically important. Kinzie (1985) recommends careful instruction about medication, frequent follow-up visits, and monitoring blood levels of medication, especially antidepressants on a monthly basis. It might also be useful to ask the patient at each visit exactly how the medication has been taken rather than assume that the patient has been compliant with instructions.

3. The clinician should be alerted to concurrent use of abusable drugs such as opium or alcohol, herbal medicine, over-the-counter medicines, or prescriptions provided by other physicians. The patient should be asked to bring in bottles of all pills at the next clinic visit.

4. The clinician should carefully avoid facile generalizations from one refugee culture to another (Lewis, 1980; Collard, 1982).

5. The clinician should be aware that variation among individuals within any given culture is greater than variation from one culture to another, and that the major variations in response are quantitative rather than qualitative.

6. Clinicians should consider other therapies in conjunction with medication, including other somatic treatment such as acupuncture, hypnosis, relaxation, as well as counseling. In addition, the clinicians need to know when not to treat with medication and instead to rely only on these other therapies. In general, if the patient's symptoms are of relatively recent onset or are not disabling, then non-medical intervention may be more appropriate. Diagnostically, many of these patients have an adjustment disorder, anxiety symptoms, or dysthymia, without the vegetative symptoms of major depression such as sleep or appetite disturbance. Other therapies should also be considered for patients who refuse to take increased dose of medications or are otherwise resistant to improving. More intensive programs such as day treatment or inpatient hospitalization may be necessary for such patients.

7. Treatment recommendations for refugees vary depending upon the experiences of the clinician. Among the variables accounting for such differences are the specific refugee groups treated, the length of time since their arrival in the United States, the severity of their illnesses, and the personal preferences of the treating psychiatrist. The author recommends judicious use of medications from all categories and generally initiates treatment at doses far lower than recommended for Westerners.

A. DEPRESSIVE SYMPTOMS

In depression, a major target symptom is insomnia, for which one of the more sedating antidepressants is the drug of choice. The author recommends trazodone (Desyrel) 50 mg at night, or amitriptyline (Elavil) 10 to 25 mg at night, increasing as tolerated for several weeks unless side effects are unacceptable to the patient. Some clinicians feel uncomfortable prescribing trazodone because of reported priapism in males. Alternatively, alprazolam (Xanax) 0.25 mg at night is often helpful for sleep. For those patients without significant sleep disturbance, a starting dose of imipramine (Tofranil) 10 mg three times per day may control symptoms of both anxiety and depression. If the anticholinergic side effects of amitriptyline or imipramine are not tolerated, nortriptyline 25 mg at night may be the drug of choice. Kinzie recommends starting Southeast Asian patients on imipramine 50 mg at night, increasing to 150 mg in three weeks, and taking a blood level in one month. Westermeyer recommends increasing increments of 50 to 75 or 100 mg and taking a blood level in one month. For treatment of refractory psychotic depression, especially in Cambodian women,

Westermeyer recommends electroconvulsive therapy if several months of outpatient treatment have failed and if symptoms such as hallucinations persist.

If side effects are not tolerated by the patient, (Kinzie, 1985) recommends changing the medication after a one month trial. Others recommend increasing a given medication until standard therapeutic blood levels are reached before switching to an alternative medication. Among the most disturbing aspects of these anticholinergic side effects for many Southeast Asians is their interpretation that their body's hot/cold balance is altered.

B. ANXIETY SYMPTOMS

Anxiety symptoms, including panic attacks, can be treated with small doses of alprazolam or imipramine, increasing as tolerated. Post-traumatic stress disorder, according to Kinzie (Gold Award, 1986), can be treated with a combination of clonidine (Catapres), which is used primarily to treat hypertension, and imipramine. This is particularly effective in controlling the symptoms of hyperarousal. Kinzie starts with imipramine and treats for one or two months until adequate blood levels are reached, then adds clonidine if hyperarousal symptoms persist. He finds that clonidine is well tolerated because of the relatively few side effects. Kinzie uses the dosages recommended for treatment of hypertension, starting at 0.1 mg twice a day and increasing to three times a day. Clonidine affects the peripheral nervous system, decreaseing hyperarousal in addition to blood pressure by the mechanism of norepinephrine reduction. For patients who have particular problems with medication compliance, Kinzie recommends using seven day "patches" for long acting release of the medication.

Antidepressant medications such as monoamine oxidase inhibitors (MAOIs) or trazodone have also been used. Trazodone given at night often helps the insomnia and nightmares as well as controlling symptoms of anxiety and depression during the day. Both trazodone and carbamazepine (Tegretol) also have some effectiveness in controlling behavioral outbursts.

C. PSYCHOTIC SYMPTOMS

For psychotic symptoms, Kinzie (1985) recommends perphenazine (Trilafon), using relatively high doses for acute stabilization but much lower doses, compared with Americans, for maintenance. Kinzie feels that the side effect profile of perphenazine is more easily tolerated in the Southeast Asians he treats. If medication compliance presents such a problem, however, Kinzie (1985) has been using potent long acting neuroleptics such a fluphenazine (Prolixin) or haloperidol (Haldol). For many chronic schizophrenics, Kinzie is now recommending fluoxetine (Prozac) which has relatively few side effects and requires only a single morning dose each day.

In bipolar affective disorder, lithium may be used for maintenance. Blood levels, at least for Asians, may not need to be as high as for Westerners in order to achieve therapeutic responses (Takahashi, 1979; Yang, 1985). Levels in the range of 0.5 mEq/l may be effective.

RECOMMENDATIONS FOR RESEARCH NEEDS AND STRATEGIES

There is a pressing need for more clinical knowledge to refine guidelines for treatment based upon well-controlled clinical psychiatric studies rather than upon the experience of those working in the field of refugee mental health. These studies need to incorporate newer methodologies in cross-cultural diagnosis, assessment, rating instruments, as well as newer laboratory and statistical developments.

In particular, rates of compliance with prescribed medications are needed. Comparisons of interventions to maximize compliance, such as education of the patient and family or use of medications with fewer side effects are also needed. Treatment strategies for special diagnostic entities or presentations, including "cultural bound" syndromes, chronic post traumatic stress disorder, paranoia, and dysthymia would be extremely helpful. We need comparisons of which medications work for certain refugees with particular diagnoses under defined conditions.

In addition to these "in vivo" studies, however, we also need to pursue biological psychopharmacology or "in vitro" studies of differences between refugee groups. Unfortunately, even though most of the refugees to the U.S. are from Southeast Asia, the majority of the literature discussing pharmacologic differences among ethnic groups reports studies of Asian groups to which very few refugees belong.

Factors which may account for ethnic differences in pharmacokinetics include genetically determined variations in microsomal oxidation, conjugation, or acetylation. However, many of these differences,

especially in oxidation, can also be affected by environmental factors such as diet, nutrition, climate, atmospheric pollution, cigarette smoking, and previous exposure to other drugs or food additives. Biodemographic factors such as the economic state of the individual, the educational level, and the time since arrival in the country of final resettlement may correlate with these environmental variables and thus influence the pharmacokinetics. Methodologically, conducting such research is difficult because of the need for 1) diagnostic consistency across cultures, including comparability of assessment instruments and measurement of cognitive processes, 2) comparability of samples for severity and chronicity of psychiatric illness, 3) standardization by body weight and per cent body fat, or 4) use of liquid preparations of medications since tablets can be affected by gastric Ph and motility, interfering with the bioavailability of the active ingredients. Laboratory methodologic problems include 1) the lack of standardization across laboratories, 2) the need to consider ethnic variations in protein binding of the medications, and 3) differences in single or multiple dose measurements. Both parent drugs and active metabolites need to be accounted for and, for antipsychotic medications, a radioreceptor assay for dopamine blocking activity in the serum may be needed. Clearance rate markers, such as debrisoquin, which marks hydroxylation status, may be necessary in studies of antidepressant medication.

Research should consider the methodological differences and large number of possible genetic and environmental determinants. Study design involving single dose kinetics of normal volunteers are much easier to conduct and, although they may provide valuable information, the results

may not be applicable to clinical populations. Clearly large numbers of patients, probably from several programs around the country, will be necessary in order to control for the large number of variables. Not only must the refugee groups studied be ethnically homogeneous, but medication using each possible metabolic enzyme pathway is needed in order to allow for generalizability. Recent developments in statistical analytic methods may enable researchers to properly analyze large data sets collected in clinical settings. One strategy is the use of Bayesian statistics of clinical samples from which medication blood levels are drawn for steady state doses and for which clinical outcome is measured. In view of the importance and complexity of these issues, careful collaborative research is needed.

Conclusions

This paper has attempted to briefly overview issues and findings in the use of psychotherapeutic medications to treat refugees. The issues are complex and the findings in the literature are often inconclusive.

For those within any ethnic or refugee population, there is considerable overlap of individual medication responses with individuals from groups used for comparison. However, for many of the ethnic groups to which refugees belong, there is evidence that responses to medication differ quantitatively from the responses of mainstream Caucasian Westerners. These differences can be due to a variety of genetic, environmental, psychological, or socio-cultural factors. For refugees, the experiences of forced migration and traumatic stress complicate the possible explanations.

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Table 1

INDOCHINESE EXPECTATION OF HEALERS
AND ROLES OF AMERICAN PHYSICIANS

Indochinese expectations and needs of healer/physician	American physician's Expected roles and duties
Expects healer to understand illness or problems	Actively involved in diagnosis
Needs explanation of illness in understandable terms	Gives firm concept of etiology and education
Wants active treatment to reduce symptoms or cure	Actively involved in treatment, often with medicine
Expects rapid cure--hope in medicine	Goal: to reduce symptoms or cure illness
Often needs to have sick role confirmed	Confirms the sick role
Needs to have family stress, fear, and guilt reduced	Prevents anyone from being blamed or misfortune

Adapted from Kinzie, 1985
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TABLE 2

CHARACTERISTIC FEATURES OF
TRADITIONAL AND MODERN MEDICINE

	Medical Systems	
CHARACTERISTIC FEATURES	Traditional	Modern
Primary cause of disease	Supernatural	physical
Psychosomatic components of disease	important	relatively unimportant
Diagnosis of disease	by divination	by physical examination
Role of ritual incantations and sacrifice in cure	important	unimportant
Role of pharmacologically active ingredients medication	relatively unimportant	important
Dosage of remedy	relatively unimportant	strictly regulated
Time interval between doses	not regulated	strictly regulated
Length of treatment	normally relatively short	variable but can be for life
Iatrogenic Disease (due to medication)	unknown	important

Adapted from Okpaku, 1986
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